Cirne *et al. Cardio-Oncology* (2025) 11:28
https://doi.org/10.1186/s40959-025-00322-9

Cardio-Oncology

CORRESPONDENCE Open Access

Principles of optimal multidisciplinary management of prostate cancer in clinical practice

Filipe Cirne[1], Michiel Sedelaar[2], Vivek Narayan[3], Ariane Macedo[4,5], Christopher Koo[6], Jeffrey de Jesus[7], Anthony Ng[8], Diogo Bastos[9], Alberto Briganti[10], Susan F. Dent[11,12], Nishant P. Shah[13,14], Renato D. Lopes[13,14,16*], Daniel J. Lenihan[15] and Darryl P. Leong[1]

Abstract

Advances in the diagnosis and management of prostate cancer have significantly changed the disease landscape. While benefiting from better oncological outcomes, patients are now experiencing higher rates of non-cancer comorbidities, including cardiovascular disease. The increasing impact of cardiovascular disease in those with prostate cancer led to the expanding role of cardio-oncology professionals in enhancing the multidisciplinary care of these patients. As a result, the International Cardio-Oncology Society (IC-OS) launched a 4-webinar series in collaboration with the European Association of Urology and the Canadian Urology Association to inform best practices in the multidisciplinary care of patients with prostate cancer. This program highlighted currently recommended diagnostic and treatment strategies from urology, oncology, and cardiology and emphasized knowledge gaps and future directions. In this article, which is the second in a 2-part series, we review challenging cases that were presented and discussed among a multidisciplinary international panel and highlight ongoing research and future directions from both urology/oncology and cardio-oncology.

Keywords Prostate cancer, Cardiovascular disease, Cardio-oncology, Multidisciplinary care

*Correspondence:
Renato D. Lopes
renato.lopes@duke.edu
[1]Department of Medicine and Population Health Research Institute, McMaster University, Hamilton, Canada
[2]Department of Urology, Radboud University Medical Center, Nijmegen, The Netherlands
[3]Department of Medicine, Division of Hematology-Oncology, University of Pennsylvania, Philadelphia, PA, USA
[4]Hospital Samaritano, São Paulo, Brazil
[5]Brazilian Clinical Research Institute, São Paulo, Brazil
[6]Beth Israel Deaconess Medical Center, Boston, MA, USA
[7]St. Luke's Medical Center Global City, Taguig, Philippines
[8]Department of Surgery, The Chinese University of Hong Kong, Shatin, Hong Kong, China
[9]Department of Medical Oncology, Hospital Sirio Libanes, São Paulo, Brazil
[10]Vita-Salute San Raffaele University, Milan, Italy
[11]Division of Medical Oncology, Department of Medicine, Duke University School of Medicine, Durham, NC, USA
[12]Duke Cancer Institute, Duke University School of Medicine, Durham, NC, USA
[13]Division of Cardiology, Department of Medicine, Duke University School of Medicine, Durham, NC, USA
[14]Duke Clinical Research Institute, Duke University School of Medicine, Durham, NC, USA
[15]Department of Medicine, Washington University School of Medicine, St. Louis, MO, USA
[16]Duke Clinical Research Institute, P.O. Box 17969, Durham, NC 27715, USA

Introduction

Advances in the diagnosis and management of prostate cancer have significantly changed the disease landscape. While benefiting from better oncological outcomes, patients are now experiencing higher rates of non-cancer comorbidities, including cardiovascular disease. Shared risk factors (e.g., age), improved cancer survival (longer exposure to other comorbidities and risk factors), and metabolic disturbances from anti-androgen therapy (ADT) put patients with prostate cancer at increased risk for cardiovascular disease [1]. Data from the SEER database show cardiovascular disease to be the major cause of death in patients with non-metastatic prostate cancer and the second most frequent cause in those with metastatic disease [2].

The increasing impact of cardiovascular disease in those with prostate cancer led to the expanding role of cardio-oncology professionals in enhancing the multidisciplinary care of these patients. As a result, the International Cardio-Oncology Society (IC-OS) launched a 4-webinar series in collaboration with the European Association of Urology and the Canadian Urology Association to inform best practices in the multidisciplinary care of patients with prostate cancer. This program highlighted currently recommended diagnostic and treatment strategies from urology, oncology, and cardiology and emphasized knowledge gaps and future directions. In this document, we discuss the last 2 webinars in the series. In webinar 3, challenging cases were presented and discussed among a multidisciplinary international panel. Webinar 4 focused on ongoing research and future directions from both urology/oncology and cardio-oncology.

Collaborative practice in prostate cancer: how is this actually done?

Not infrequently, patients with advanced prostate cancer have concomitant complex cardiovascular disease or even multiple cardiovascular conditions that might need to be actively managed throughout their cancer survivorship journey. The following illustrative real-world clinical cases were discussed in the webinars: (1) a patient with high-grade stage III prostate cancer and diabetes who was a current smoker with asymptomatic multivessel coronary artery disease (CAD) and significant ischemia on non-invasive functional testing; (2) a patient with de novo prostate cancer (Gleason score 9 [5 + 4]) who was being managed with ADT, had multiple cardiovascular risk factors, had established systemic atherosclerosis with peripheral artery disease (infra-renal abdominal aortic aneurysm not fulfilling surgical criteria), and had New York Heart Association class II heart failure associated with new, severe left ventricular dysfunction in the context of significant progression of CAD; and (3) a patient who was post-prostatectomy for Gleason score 10 prostate cancer on adjuvant ADT and had chronic obstructive pulmonary disease, hypertension, type 2 diabetes, endovascular aneurysm repair for abdominal aortic aneurysm, prior percutaneous coronary intervention for acute coronary syndrome, and on antithrombotic therapy complicated by multiple bleeding events. These cases make evident the complexities of managing treatment for this patient population.

Cardiovascular risk factors are common and frequently poorly controlled in men with prostate cancer. In a cross-sectional analysis of 90,494 men with prostate cancer treated in the U.S. Veterans Health Administration, 54.1% had uncontrolled risk factors; of these, 29.6% were not receiving risk-reducing medication [3]. In a recent analysis of the ongoing RADICAL-PC study, Klimis et al. showed that among 2811 consecutive patients with prostate cancer being followed prospectively, 99% had at least 1 uncontrolled cardiovascular risk factor, and 51% had at least 3 uncontrolled cardiovascular risk factors [4].

Additionally, atherosclerotic cardiovascular disease is common among patients with prostate cancer. Data from a Korean administrative database showed the prevalence and incidence of cardiovascular disease in patients with prostate cancer were 14% and 20% over 11 years [5]. In another analysis of the RADICAL-PC study, the prevalence of established cardiovascular disease in patients with prostate cancer was 22%[6].

In this context, relevant questions pertaining to the multidisciplinary care of these patients are as follows.

When diagnoses are made concomitantly, what should be treated first, prostate cancer or CAD?

An important consideration for addressing this question is the prostate cancer prognosis. High-grade prostate cancer carries a high risk for disease progression despite local therapy, with 10-year rates for progression to metastatic disease of 24–28%[7, 8] In contrast, lower-risk patients may benefit from treatment of cardiovascular morbidities first before definitive prostate cancer therapy. Ultimately, the decision as to which condition should be treated first will need to be made in a multidisciplinary manner including the patient, uro-oncologist, interventional proceduralist and cardio-oncologist [9]. Factors playing into this decision, other than prostate cancer risk, include the magnitude and the immediacy of benefit conferred by the cardiovascular intervention, the potential for complications from the cardiovascular intervention as well as patient preferences. Complications from invasive cardiac procedures may lead to undesirable delays in prostate cancer therapy. In addition, the requirement for dual antiplatelet therapy following percutaneous coronary intervention may complicate the timing of prostatectomy or predispose to hemorrhagic complications such as radiation proctitis following

radiotherapy. Nonetheless, cardiac interventions such as primary percutaneous coronary intervention for high-risk myocardial infarctions are likely to confer important and rapid symptomatic and prognostic benefits and recent evidence suggests that dual antiplatelet therapy can be de-escalated earlier than previously thought safe. In cases where coronary artery bypass surgery is under consideration, the lengthy recovery time maybe incompatible with prostatectomy except in low-risk or intermediate-risk prostate cancer with favourable characteristics. However, treatment recommendations when coronary artery bypass surgery is an alternative must be individualised based on coronary anatomy, the feasibility of percutaneous coronary strategies as well as radiotherapy or active surveillance for the cancer, and patient characteristics such as frailty and surgical risk.

In the setting of stable multivessel CAD, should revascularization be added to optimal medical therapy, and, if so, what is the best revascularization strategy?

In the management of stable CAD, the ISCHEMIA trial showed that, in the general population, an initial invasive strategy (including coronary angiography and revascularization, when feasible) is not superior to a conservative strategy (medical therapy alone and coronary angiography if medical therapy fails) in reducing cardiovascular death, myocardial infarction, hospitalization for unstable angina or heart failure, or resuscitated cardiac arrest even with moderate to severe ischemia on functional tests, provided no left main disease or moderate left ventricular dysfunction are present. Patients with cancer were probably not well represented, as one of the exclusion criteria was life expectancy less than 5 years due to non-cardiovascular comorbidity [10]. However, there are now many pharmacologic strategies to prevent the progression of atherosclerotic vascular disease, including statins, ezetimibe, antiplatelet agents, beta-blockers, low-dose rivaroxaban, proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors, sodium-glucose cotransporter-2 (SGLT2) inhibitors, and glucagon-like peptide 1 (GLP-1) receptor agonists.

If surgical oncological interventions are indicated, how should antithrombotic therapy be managed?

Uncertainty exists when managing antiplatelet therapy in patients with prostate cancer and other urological malignancies with potential for bleeding from hematuria or perioperative bleeding. Limited data concerning best dual antiplatelet therapy (DAPT) management strategies for patients with urological malignancies are available. Until personalized data to support best practices in this scenario exist, multidisciplinary team discussion including the patient is a reasonable strategy. Additionally, although not specifically validated in the prostate cancer population, bleeding and ischemic risk scores can be used as adjunctive tools (e.g., DAPT score, PRECISE-DAPT score) [11, 12].

When should patients with prostate cancer be referred to a cardiologist or cardio-oncologist?

Evidence demonstrating the suboptimal treatment of cardiovascular risk factors in patients with prostate cancer suggests that some of these individuals may benefit from strategies to optimize cardiovascular risk factor control, potentially by referral to a cardiologist or cardio-oncologist. Given the adverse effects of ADT on cardiovascular risk factors, those receiving ADT may stand to benefit most. However, several factors influence referral practice, including local/regional infrastructure. Primary prevention scores, like the Framingham Risk Score, Systematic Coronary Risk Evaluation 2 (SCORE2), and Atherosclerotic Cardiovascular Disease (ASCVD) risk score, might be useful tools aiding referral decisions and are endorsed by the 2022 European Society of Cardiology (ESC) guidelines on cardio-oncology. However, these scores have not been validated in the prostate cancer population. In addition, patients with known CAD might be good candidates for cardio-oncology referral [13].

Should the presence of atherosclerotic cardiovascular disease influence ADT strategies?

In a large, retrospective, single-centre study of patients receiving radiotherapy with or without neoadjuvant ADT, those treated with ADT who had no comorbidities or at most a single coronary artery disease risk factor were at a similar mortality to those not receiving ADT [14]. However, those with a history of myocardial infarction or ischemic cardiomyopathy more at a 2-fold higher risk of all-cause mortality if they were treated with ADT. Despite this evidence, the causal role of ADT remains incompletely defined and optimal cardiovascular risk factor management may mitigate any adverse cardiovascular effects of ADT. Therefore, in our view, the decision to administer ADT should predominantly be based on cancer characteristics rather than the presence of cardiovascular risk factors, while these risk factors should be monitored and addressed.

Regarding the choice of ADT therapy, the 2022 ESC guidelines recommend a gonadotropin-releasing hormone (GnRH) antagonist be considered over a GnRH agonist in patients with pre-existing symptomatic CAD (COR IIa, LOE B) [13]. A meta-analysis of randomized clinical trials showed that GnRH antagonists are associated with a 43% lower risk for adverse cardiovascular events, 51% lower risk for cardiovascular death, and 52% lower risk for all-cause mortality compared with GrRH agonists. However, these data are not robust, owing to the lack of blinding and pre-specification of cardiovascular

outcomes, making this a weak recommendation [15]. More recently, Lopes et al. published the results of the PRONOUNCE trial, comparing the cardiovascular safety of the GnRH antagonist degarelix with the GnRH agonist leuprolide. This was the first international, randomized trial assessing major cardiovascular events as the primary outcome (composite of death, myocardial infarction or stroke) in men with prostate cancer being treated with different ADT drug classes. Unfortunately, because of slower-than-projected enrollment and fewer-than-projected primary outcome events, the trial was stopped before the 900 planned participants were accrued, making the study underpowered and thus leaving the question unanswered [16]. REPLACE-CV (NCT05605964) and REVELUTION (NCT05320406) are 2 ongoing randomized clinical trials comparing the oral GnRH antagonist relugolix with the GnRH agonist leuprolide, with cardiovascular outcomes pre-specified.

Ongoing clinical research in prostate cancer: what can we anticipate?

Urological/oncological perspective

Perioperative treatment intensification Prostate-specific membrane antigen (PSMA) positron emission tomography (PET) has an increasing role in the identification of micro-metastatic disease. While 37% of patients with very high-risk prostate cancer (Gleason score ≥ 8 and prostate-specific antigen [PSA] > 20 ng/mL) at diagnosis have evidence of metastases on skeletal axial magnetic resonance imaging (MRI), 24% of those at high risk have upstaging by PSMA PET/computed tomography (CT) [17, 18].

There are several studies of neoadjuvant ADT in this setting. They have yet to show a benefit of such a strategy on clinical endpoints (e.g., clinical recurrence, survival) [19]. Possible reasons for neoadjuvant ADT failure are faulty patient selection that includes intermediate-risk patients with prostate cancer, underpowered studies, short length of follow-up, or possibly incomplete androgen tissue suppression, which could be overcome by more intensive regimens. This last hypothesis is being tested in phase 2 and phase 3 trials with the addition of androgen receptor signaling inhibitors (ARSIs) (such as abiraterone, enzalutamide, apalutamide, darolutamide, and even double ARSI) to conventional ADT therapy [20]. The largest trial in this setting still to be published is the PROTEUS trial (NCT03767244), which is a phase 3 multicenter trial testing the use of apalutamide + ADT compared with placebo + ADT alone prior to radical prostatectomy. Moreover, other ongoing studies are testing different drugs and combinations in the neoadjuvant setting, such as ibrutinib (NCT02643667); apalutamide, abiraterone acetate, prednisone, degarelix, and indomethacin (NCT02849990); cabazitaxel, docetaxel, mitoxantrone, or satraplatin (NCT03258320); rituximab (NCT01804712); trametinib and dasatinib (NCT01990196); pazopanib (NCT01832259); and olaparib (NCT02324998).

Studies assessing the usefulness of radiotherapy pre- and/or post-radical prostatectomy are also underway. In the neoadjuvant setting, the use of the radionuclide lutetium-177 (^{177}Lu)–PSMA-617 is being tested in phase 1 trials with patients with high-risk localized disease [21, 22]. Initial reports showed that the absorption of the radionuclide by the prostatic tissue is clinically meaningful, but pathological responses have been disappointing so far [22].

The future of perioperative therapy intensification in prostate cancer may not be a one size fits all approach but rather individualized based on precision medicine. A tailored approach according to patients' specific profiles, including individual mutations, may prove important.

Metastasis-directed therapies in metastatic hormone-sensitive prostate cancer Patients with metastatic hormone-sensitive prostate cancer (mHSPC) are increasing in numbers. New imaging modalities, such as PSMA PET/CT, have greatly enhanced our capacity to diagnose these patients at an earlier point in the disease course. These individuals can present with low-burden oligo-metastatic prostate cancer [23] that may be classified as synchronous versus metachronous (recurrent) oligometastatic disease. There are limited data on how to manage oligo-metastatic disease [24].

In the setting of metachronous mHSPC, initial evidence suggests a potential benefit in targeting distant disease deposits seen on imaging [25]. In this context, ADT, surgery, and stereotactic ablative surgery (SABR) have all been tested in randomized clinical trials and have been shown to improve cancer-related outcomes [26–28].

Even though there seems to be an added benefit of targeting the distant disease deposits, the best strategy is still not known as comparisons have been limited. Some other questions still to be addressed in future studies are as follows.

- Can/should radiotherapy be delivered with different doses and volumes?
- Does the use of modern imaging improve outcomes?
- What is the role of germline-changing systemic therapies?
- What other information about tumor biology can impact care of patients with prostate cancer?

The PRIMORDIUM study (NCT04557059), which will consist of an interventional arm and prospective cohort arms, may provide additional insights in the setting of

metachronous disease. In its interventional arm, patients with a positive PSMA PET will be randomized to receive salvage radiotherapy + GnRH agonist ± apalutamide. The primary endpoint will be the time from randomization until PSMA PET distant metastatic progression or death from any cause. The observational arm is planned to investigate natural history of recurrent mHSPC with a negative PSMA PET as well as to obtain information on management, imaging, and additional outcomes.

PSMA ligand therapy PSMA is highly expressed in metastatic castration-resistant prostate cancer. ^{177}Lu–PSMA-617 is a radioligand therapy that delivers beta-particle radiation to PSMA-expressing cells and the surrounding microenvironment. Based on improvements in overall survival and progression-free survival seen in the VISION trial, the 2022 European Association of Urology Guidelines on Prostate Cancer strongly recommend offering ^{177}Lu–PSMA-617 to pre-treated patients with mCRPC with ≥1 metastatic lesions highly expressing PSMA (exceeding the uptake in the liver) [24, 29]. While some patients might not respond due to heterogeneity of tumor PSMA expression, tumor mutational factors, distribution of disease, and failure to deliver a lethal radiation dose, initial evidence suggests concomitant use of ADT, immunotherapy, and poly (ADP-ribose) polymerase (PARP) inhibitors are promising approaches [29–34].

Cardio-oncology perspective

What lessons can we learn from breast cancer? Over the last decade, significant improvements in oncologic outcomes have been seen for both prostate and breast cancer. The 5-year survival rate for breast cancer now exceeds 90%, with the survival rate for localized disease being nearly 99%. However, as with patients with prostate cancer, most patients with breast cancer have at least 1 cardio-metabolic comorbidity, such as hypertension, diabetes, or dyslipidemia, at the time of their diagnosis. This seems to be particularly important considering that population-based data suggest that women who survive having breast cancer are at greater risk for cardiovascular disease mortality than women without breast cancer [4, 35–37]. Similarly, cardiovascular disease mortality is the leading cause of death in patients with prostate cancer [36, 38, 39]. This highlights the fact that, as for breast cancer, physicians are effectively treating the oncological issues of patients with prostate cancer, but there is a need for improvement in managing cardiovascular morbidity.

Albeit by different agents and mechanisms, cancer therapies seem to drive some of the increased risk for cardiovascular disease in the prostate and breast cancer populations. While cardiovascular and metabolic complications in prostate cancer appear to increase because of ADT, in breast cancer these complications are linked to the utilization of anthracyclines, anti-HER2 agents, chest radiotherapy, aromatase inhibitors, and selective estrogen receptor modulators [40–49]. Moreover, there have been small trials of cardioprotection and studies on toxicity surveillance in breast cancer, but similar evidence is still to be found in the prostate cancer population [50, 51].

Despite available data suggesting a high incidence of cardiovascular disease in patients with prostate or breast cancer, risk prediction models have only been derived and validated in breast cancer [6, 52–57]. Therefore, there is an obvious unmet need for developing similar or even more aggressive cardiovascular prevention and treatment strategies for those with prostate cancer.

To facilitate the management of cancer and non-cancer therapy, a team-based approach is paramount. Shared responsibilities among oncology, primary care, and cardiovascular care teams are effective communication, prevention of frailty, appropriate use of technology, judicious use of financial resources, and communication/discussion about research opportunities. In addition, while physicians play a major role in the circle of care, non-physician professionals, such as psychologists, dieticians, social workers, and the family and caregivers, are just as important and should be active members in the decision-making process [58].

There is a paucity of evidence-based recommendations for the management of comorbidities among those who survive having cancer. Existing strategies are extrapolated from existing guidelines intended for populations without cancer [58]. Analogous to the recommendations made for patients with prostate cancer on ADT, the 2022 ESC guidelines on cardio-oncology advocate for baseline cardiovascular risk assessment with scores derived from the general population (e.g., SCORE2) and periodic cardiovascular surveillance in those with breast cancer on endocrine therapy [13].

Enhancing survival of cardiovascular disease and prostate cancer As a complex and evolving concept, the definition of surviving cancer has changed over time. Some consider it to be survival ≥ 5 years after diagnosis, while others, such as the National Coalition for Cancer Survivorship, use broader definitions like "from cancer diagnosis to end of life." However, some individuals who have had cancer do not agree with the "survivor" moniker, refusing to let the cancer define them [59, 60]. Alternatively, rather than trying to apply a definition to surviving cancer, the American Cancer Society acknowledges different trajectories in those who are cancer free and in those with active cancer (Table 1).

When treating patients with prostate cancer, it is imperative to consider the different management

Table 1 Cancer trajectories according to the American Cancer Society

Cancer Free	With Cancer
For the remainder of life	With intermittent periods of active disease needing treatment
For years but with complications of cancer therapy	Continuously with cancer
For years with late cancer recurrence	
With the possibility of developing a second cancer (or other competing risk)	

strategies depending on patient and cancer characteristics, which can include active surveillance, definitive therapy, or watchful waiting. Patients may have remission from prostate cancer, but there is still a risk of biochemical relapse and development of metastatic disease, both with significant morbidity and treatment implications. Competing risks and ultimately death can occur at any time during the disease course. While it is a cornerstone for the treatment of advanced prostate cancer, ADT can impact many aspects of surviving prostate cancer (Fig. 1).

ADT has been associated with adverse effects with potentially substantial implications in quality of life, including fatigue, loss of muscle strength, fat gain, depression, cognitive decline, and erectile dysfunction. However, the strength of the evidence supporting these associations is modest. This is particularly concerning considering that up to 40% of men with prostate cancer will receive ADT at some point during their cancer treatment, so the aforementioned side effects could affect a considerable proportion of patients with a very common cancer. Interestingly, many of these complications are found in those with cardiovascular disease as well, highlighting the overlap in terms of quality of life and other adverse effects in prostate cancer and cardiovascular disease.

From a body composition perspective, a small study by Smith et al. showed significant increases in weight and waist circumference over the course of 12 months in 26 men with prostate cancer receiving leuprolide [61]. An important limitation of this study was the lack of a control group, which prevented the researchers from ruling out the possibility of these increases in weight and waist circumference being related to lifestyle or prostate cancer in general. Furthermore, these findings do not necessarily correlate with the loss of muscle strength and/or mass. Data from the PURE study show that low muscle strength is associated with higher mortality in those who develop a wide range of conditions, including myocardial infarction, stroke, cancer, and respiratory disorders. In addition, every 5 kg decrease in handgrip strength was associated with a 16% higher risk for all-cause mortality, 7% higher risk for myocardial infarction, and 9% higher risk for stroke [62]. In this context, unpublished

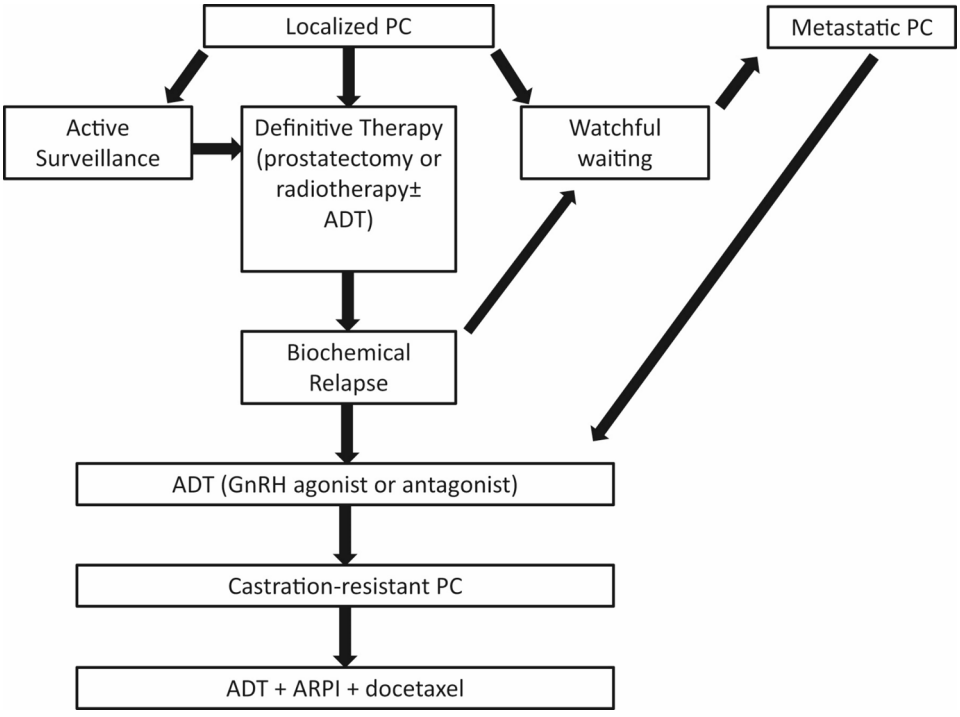

Fig. 1 Treatment strategies for prostate cancer.
Source: Reprinted with permission from: Leong DP, et al. Cardiovascular Risk in Prostate Cancer: JACC: CardioOncology State-of-the-Art Review. JACC Cardio Oncol. 2024 Nov 19;6(6):835–846. doi: https://doi.org/10.1016/j.jaccao.2024.09.012

data from the ongoing RADICAL-PC study showed that in comparison with patients not on ADT, patients with prostate cancer receiving ADT had a more pronounced increase in their waist circumference and a decrease in handgrip strength over the course of 12 months. Of note, these analyses were not adjusted for potential confounding factors such as age, level of education, ethnicity, alcohol use, tobacco use, and level of physical activity. Once the study follow-up is completed, a larger sample size will allow the RADICAL-PC investigators to repeat those analyses with an acceptable statistical power to perform those adjustments.

Metabolic changes complicating an increase in central adiposity have also been seen in men with prostate cancer receiving ADT. A large retrospective study with 12,191 men in the United States with localized prostate cancer showed a 61% higher incidence of diabetes in those receiving ADT compared with those not receiving ADT [63]. Another retrospective study from an administrative database in Taiwan showed that in 6002 men with prostate cancer, ADT was associated with a 78% higher incidence of hypertension over the course of 10 years compared with that of propensity-score matched controls [64].

Interestingly, cardiovascular risk factor control in men with prostate cancer seems to be poorly achieved and addressed despite the undesirable negative consequences of cardiovascular risk. Data from the multinational RADICAL-PC study showed poor risk factor control in 2811 men with prostate cancer when taking into consideration guidelines recommendations and thresholds [4]. High waist-to-hip ratio was seen in 91% of the participants, high blood pressure in 78%, high low-density lipoprotein cholesterol in 51%, physical inactivity in 19%, and tobacco use in 10%.

With regards to physical inactivity, even though the definitions might be somewhat arbitrary, its importance is highlighted when considering the dose-dependent effect on health outcomes. As shown by the PURE study group, an incremental risk of all-cause mortality and major cardiovascular disease was seen with decreasing levels of physical activity in 130,000 community-dwelling adults [65]. There have been several trials, with participants totaling several hundreds of men with prostate cancer, examining the effects of structured exercise programs on anthropometrics. A pooled analysis by Shao et al. with 12 randomized clinical trials and 715 participants showed that in men with prostate cancer on ADT, a structured exercise program resulted in a higher lean body mass (mean difference: 0.88, 95% confidence interval [CI] 0.40 to 1.36; $P<0.01$), lower fat mass (mean difference: -0.60, 95% CI -1.10 to -0.10; $P<0.05$) and lower body fat rate (mean difference: -0.93, 95% CI -1.39 to -0.47, $P<0.01$) relative to controls [66]. Furthermore, subgroup analyses revealed greater efficacy for exercise duration of ≥6 months (vs. <6 months) and exercise immediately after the therapy (vs. delayed exercise). Additionally, promising data from the ERASE trial showed that compared with those receiving usual care, patients with localized prostate cancer on active surveillance randomized to a high-intensity interval training program (HIIT) had a higher peak VO2, as expected, but also decreased PSA levels (-1.1 µg/L; 95% CI, -2.1 to 0.0; $P=0.04$), PSA velocity (-1.3 µg /L/y; 95% CI, -2.5 to -0.1; $P=0.04$), and LNCaP cell growth (-0.13 optical density unit; 95% CI, -0.25 to -0.02; $P=0.02$)[67]. Some important barriers to exercise in men with prostate cancer noted in clinical practice are deconditioning following definitive therapy, urinary incontinence, fatigue and weight gain from ADT, and bone pain from metastatic disease.

While sequelae of ADT affect the quality of life for those with prostate cancer, the combination of exercise, dietary counselling, preventive medications (e.g., statins), and aggressive risk factor control could be an important adjunct strategy to mitigate some of the anthropometric and metabolic adverse effects of ADT. Moving forward, it will be important understand how exercise-induced changes in body composition influence clinical outcomes, how sustainable these structured exercise programs are, and how to optimize exercise adherence specifically in the population of men with prostate cancer.

Conclusion

The success of contemporary strategies in treating prostate cancer has positively impacted the disease landscape. However, as patients survive longer, new challenges have arisen. Metastatic and castration-resistant disease are becoming progressively more common in clinical practice, but there is exciting research underway to test diagnostic and therapeutic approaches in the population experiencing such disease. Lastly, improved cancer prognosis has resulted in non-oncologic comorbidities gaining importance, with cardiovascular disease now being among the most common causes of death and morbidity. Therefore, the need for a multidisciplinary approach to prostate cancer is warranted, with the cardio-oncology professional recognized as a core member of the team.

Abbreviations

ADT	Anti-Androgen Therapy
CAD	Coronary Artery Disease
CO	Cardio-Oncology
CUA	Canadian Urology Association
CV	Cardiovascular
CVD	Cardiovascular Disease
DAPT	Dual Antiplatelet Therapy
ESC	European Society of Cardiology
EAU	European Association of Urology
GnRH	Gonadotropin-Releasing Hormone
IC-OS	International Cardio-Oncology Society
mHSPC	metastatic Hormone-Sensitive Prostate Cancer

PCa	Prostate Cancer
PSMA PET	Prostate-Specific Membrane Antigen Positron Emission Tomography
SABR	Stereotactic Ablative Surgery

Acknowledgements
Diana Steele-Jones and Elizabeth E.S. Cook, both of the Duke Clinical Research Institute, provided editorial assistance.

Author contributions
All authors contributed to the design, drafting, and critical review of the manuscript.

Funding
The webinar series was funded by Ferring Pharmaceuticals; there was no external funding for the manuscript.

Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Not relevant.

Consent for publication
Not relevant.

Competing interests
The authors declare no competing interests.

Received: 31 May 2024 / Accepted: 14 February 2025
Published online: 15 March 2025

References

1. Koene RJ, Prizment AE, Blaes A, Konety SH. Shared risk factors in cardiovascular disease and cancer. Circulation. 2016;133(11):1104–14. https://doi.org/10.1161/CIRCULATIONAHA.115.020406.
2. Weiner AB, Li EV, Desai AS, Press DJ, Schaeffer EM. Cause of death during prostate cancer survivorship: a contemporary, US population-based analysis. Cancer. 2021;127(16):2895–904. https://doi.org/10.1002/cncr.33584.
3. Sun L, Parikh RB, Hubbard RA, et al. Assessment and management of cardiovascular risk factors among US veterans with prostate cancer. JAMA Netw Open. 2021;4(2):e210070. https://doi.org/10.1001/jamanetworkopen.2021.0070.
4. Klimis H, Pinthus JH, Aghel N, et al. The burden of uncontrolled cardiovascular risk factors in men with prostate cancer: a RADICAL-PC analysis. JACC: CardioOncology. 2023;5(1):70–81. https://doi.org/10.1016/j.jaccao.2022.09.008.
5. Youn JC, Chung WB, Ezekowitz JA, et al. Cardiovascular disease burden in adult patients with cancer: an 11-year nationwide population-based cohort study. Int J Cardiol. 2020;317:167–73. https://doi.org/10.1016/j.ijcard.2020.04.080.
6. Pinthus JH, Shayegan B, Klotz L, et al. The prevalence of cardiovascular disease and its risk factors among prostate cancer patients treated with and without androgen deprivation. JCO. 2020;38(6suppl):364. https://doi.org/10.1200/JCO.2020.38.6_suppl.364.
7. Pilepich MV, Winter K, Lawton CA, et al. Androgen suppression adjuvant to definitive radiotherapy in prostate carcinoma–long-term results of phase III RTOG 85–31. Int J Radiat Oncol Biol Phys. 2005;61(5):1285–90. https://doi.org/10.1016/j.ijrobp.2004.08.047.
8. Bolla M, Van Tienhoven G, Warde P, et al. External irradiation with or without long-term androgen suppression for prostate cancer with high metastatic risk: 10-year results of an EORTC randomised study. Lancet Oncol. 2010;11(11):1066–73. https://doi.org/10.1016/S1470-2045(10)70223-0.
9. Leong DP, Cirne F, Aghel N, et al. Cardiac interventions in patients with active, Advanced Solid and Hematologic malignancies: JACC: CardioOncology State-of-the-art review. JACC CardioOncology. 2023;5(4):415–30. https://doi.org/10.1016/j.jaccao.2023.05.008.
10. Maron DJ, Hochman JS, Reynolds HR, et al. Initial invasive or conservative strategy for stable coronary disease. N Engl J Med. 2020;382(15):1395–407. https://doi.org/10.1056/NEJMoa1915922.
11. Yeh RW, Secemsky EA, Kereiakes DJ, et al. Development and validation of a prediction rule for benefit and harm of dual antiplatelet therapy beyond 1 year after percutaneous coronary intervention. JAMA. 2016;315(16):1735–49. https://doi.org/10.1001/jama.2016.3775.
12. Costa F, van Klaveren D, James S, et al. Derivation and validation of the predicting bleeding complications in patients undergoing stent implantation and subsequent dual antiplatelet therapy (PRECISE-DAPT) score: a pooled analysis of individual-patient datasets from clinical trials. Lancet. 2017;389(10073):1025–34. https://doi.org/10.1016/S0140-6736(17)30397-5.
13. Lyon AR, López-Fernández T, Couch LS, the International Cardio-Oncology Society (IC-OS). 2022 ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and: Developed by the task force on cardio-oncology of the European Society of Cardiology (ESC). Eur Heart J. 2022;43(41):4229–361. https://doi.org/10.1093/eurheartj/ehac244
14. Nanda A, Chen MH, Braccioforte MH, et al. Hormonal therapy use for prostate cancer and mortality in men with coronary artery disease-induced congestive heart failure or myocardial infarction. JAMA. 2009;302(8):866–73. https://doi.org/10.1001/jama.2009.1137.
15. Cirne F, Aghel N, Petropoulos JA, et al. The cardiovascular effects of gonadotropin-releasing hormone antagonists in men with prostate cancer. Eur Heart J Cardiovasc Pharmacother. 2022;8(3):253–62. https://doi.org/10.1093/ehjcvp/pvab005.
16. Lopes RD, Higano CS, Slovin SF, et al. Cardiovascular safety of degarelix versus leuprolide in patients with prostate cancer: the primary results of the PRONOUNCE randomized trial. Circulation. 2021;144(16):1295–307. https://doi.org/10.1161/CIRCULATIONAHA.121.056810.
17. Lecouvet FE, Geukens D, Stainier A, et al. Magnetic resonance imaging of the axial skeleton for detecting bone metastases in patients with high-risk prostate cancer: diagnostic and cost-effectiveness and comparison with current detection strategies. J Clin Oncol. 2007;25(22):3281–7. https://doi.org/10.1200/JCO.2006.09.2940.
18. Ma TM, Gafita A, Shabsovich D, et al. Identifying the best candidates for prostate-specific membrane antigen positron emission tomography/computed tomography as the primary staging approach among men with high-risk prostate cancer and negative conventional imaging. Eur Urol Oncol. 2022;5(1):100–3. https://doi.org/10.1016/j.euo.2021.01.006.
19. Kumar S, Shelley M, Harrison C, Coles B, Wilt TJ, Mason MD. Neo-adjuvant and adjuvant hormone therapy for localised and locally advanced prostate cancer. Cochrane Database Syst Rev. 2006;2006(4):CD006019. https://doi.org/10.1002/14651858.CD006019.pub2.
20. Devos G, Devlies W, De Meerleer G, et al. Neoadjuvant hormonal therapy before radical prostatectomy in high-risk prostate cancer. Nat Rev Urol. 2021;18(12):739–62. https://doi.org/10.1038/s41585-021-00514-9.
21. Dhiantravan N, Violet J, Eapen R, et al. Clinical Trial Protocol for LuTectomy: a single-arm study of the dosimetry, safety, and potential benefit of 177Lu-PSMA-617 prior to prostatectomy. Eur Urol Focus. 2021;7(2):234–7. https://doi.org/10.1016/j.euf.2020.09.021.
22. Golan S, Frumer M, Zohar Y, et al. Neoadjuvant 177Lu-PSMA-I&T radionuclide treatment in patients with high-risk prostate cancer before radical prostatectomy: a single-arm phase 1 trial. Eur Urol Oncol. 2023;6(2):151–9. https://doi.org/10.1016/j.euo.2022.09.002.
23. Zaorsky NG, Calais J, Fanti S, et al. Salvage therapy for prostate cancer after radical prostatectomy. Nat Rev Urol. 2021;18(11):643–68. https://doi.org/10.1038/s41585-021-00497-7.
24. Cornford P, van den Bergh RCN, Briers E, et al. EAU-EANM-ESTRO-ESUR-SIOG guidelines on prostate Cancer. Part II-2020 update: treatment of relapsing and metastatic prostate Cancer. Eur Urol. 2021;79(2):263–82. https://doi.org/10.1016/j.eururo.2020.09.046.
25. Connor MJ, Smith A, Miah S, et al. Targeting oligometastasis with stereotactic ablative radiation therapy or surgery in metastatic hormone-sensitive prostate cancer: a systematic review of prospective clinical trials. Eur Urol Oncol. 2020;3(5):582–93. https://doi.org/10.1016/j.euo.2020.07.004.
26. Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. Lancet. 2018;392(10162):2353–66. https://doi.org/10.1016/S0140-6736(18)32486-3.

27. Ost P, Reynders D, Decaestecker K, et al. Surveillance or metastasis-directed therapy for oligometastatic prostate cancer recurrence: a prospective, randomized, multicenter phase II trial. J Clin Oncol. 2018;36(5):446–53. https://doi.org/10.1200/JCO.2017.75.4853.
28. Phillips R, Shi WY, Deek M, et al. Outcomes of observation vs stereotactic ablative radiation for oligometastatic prostate cancer: the ORIOLE phase 2 randomized clinical trial. JAMA Oncol. 2020;6(5):650–9. https://doi.org/10.1001/jamaoncol.2020.0147.
29. Sartor O, de Bono J, Chi KN, et al. Lutetium-177-PSMA-617 for metastatic castration-resistant prostate cancer. N Engl J Med. 2021;385(12):1091–103. https://doi.org/10.1056/NEJMoa2107322.
30. Purohit NK, Shah RG, Adant S, Hoepfner M, Shah GM, Beauregard JM. Potentiation of 177Lu-octreotate peptide receptor radionuclide therapy of human neuroendocrine tumor cells by PARP inhibitor. Oncotarget. 2018;9(37):24693–706. https://doi.org/10.18632/oncotarget.25266.
31. Paschalis A, Sheehan B, Riisnaes R, et al. Prostate-specific membrane antigen heterogeneity and DNA repair defects in prostate cancer. Eur Urol. 2019;76(4):469–78. https://doi.org/10.1016/j.eururo.2019.06.030.
32. Emmett L, Crumbaker M, Ho B, et al. Results of a prospective phase 2 pilot trial of 177Lu-PSMA-617 therapy for metastatic castration-resistant prostate cancer including imaging predictors of treatment response and patterns of progression. Clin Genitourin Cancer. 2019;17(1):15–22. https://doi.org/10.1016/j.clgc.2018.09.014.
33. Aggarwal RR, Luch Sam S, Koshkin VS, et al. Immunogenic priming with 177Lu-PSMA-617 plus pembrolizumab in metastatic castration resistant prostate cancer (mCRPC): a phase 1b study. JCO. 2021;39(15suppl):5053. https://doi.org/10.1200/JCO.2021.39.15_suppl.5053.
34. Gafita A, Marcus C, Kostos L, Schuster DM, Calais J, Hofman MS. Predictors and real-world use of prostate-specific radioligand therapy: PSMA and beyond. Am Soc Clin Oncol Educ Book. 2022;42:1–17. https://doi.org/10.1200/EDBK_350946.
35. Bradshaw PT, Stevens J, Khankari N, Teitelbaum SL, Neugut AI, Gammon MD. Cardiovascular disease mortality among breast cancer survivors. Epidemiology. 2016;27(1):6–13. https://doi.org/10.1097/EDE.0000000000000394.
36. Sturgeon KM, Deng L, Bluethmann SM, et al. A population-based study of cardiovascular disease mortality risk in US cancer patients. Eur Heart J. 2019;40(48):3889–97. https://doi.org/10.1093/eurheartj/ehz766.
37. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2019. Cancer J Clin. 2019;69(1):7–34. https://doi.org/10.3322/caac.21551.
38. Thomsen FB, Sandin F, Garmo H, et al. Gonadotropin-releasing hormone agonists, orchiectomy, and risk of cardiovascular disease: semi-ecologic, nationwide, population-based study. Eur Urol. 2017;72(6):920–28. https://doi.org/10.1016/j.eururo.2017.06.036.
39. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70(1):7–30. https://doi.org/10.3322/caac.21590.
40. Viani GA, Afonso SL, Stefano EJ, De Fendi LI, Soares FV. Adjuvant trastuzumab in the treatment of her-2-positive early breast cancer: a meta-analysis of published randomized trials. BMC Cancer. 2007;7(1):153. https://doi.org/10.1186/1471-2407-7-153.
41. Chen T, Xu T, Li Y, et al. Risk of cardiac dysfunction with trastuzumab in breast cancer patients: a meta-analysis. Cancer Treat Rev. 2011;37(4):312–20. https://doi.org/10.1016/j.ctrv.2010.09.001.
42. Leung HWC, Chan ALF. Trastuzumab-induced cardiotoxicity in elderly women with HER-2-positive breast cancer: a meta-analysis of real-world data. Expert Opin Drug Saf. 2015;14(11):1661–71. https://doi.org/10.1517/14740338.2015.1089231.
43. McGowan JV, Chung R, Maulik A, Piotrowska I, Walker JM, Yellon DM. Anthracycline chemotherapy and cardiotoxicity. Cardiovasc Drugs Ther. 2017;31(1):63–75. https://doi.org/10.1007/s10557-016-6711-0.
44. Matthews A, Stanway S, Farmer RE, et al. Long term adjuvant endocrine therapy and risk of cardiovascular disease in female breast cancer survivors: systematic review. BMJ. 2018;363:k3845. https://doi.org/10.1136/bmj.k3845.
45. Iacovelli R, Ciccarese C, Bria E, et al. The cardiovascular toxicity of abiraterone and enzalutamide in prostate cancer. Clin Genitourin Cancer. 2018;16(3):e645–53. https://doi.org/10.1016/j.clgc.2017.12.007.
46. Hu JR, Duncan MS, Morgans AK, et al. Cardiovascular effects of androgen deprivation therapy in prostate cancer: contemporary meta-analyses. Arterioscler. Thromb Vasc Biol. 2020;40(3):e55–64. https://doi.org/10.1161/ATVBAHA.119.313046.
47. Guo Y, Dong X, Yang F, et al. Effects of radiotherapy or radical prostatectomy on the risk of long-term heart-specific death in patients with prostate cancer. Front Oncol. 2020;10:592746. https://doi.org/10.3389/fonc.2020.592746. eCollection 2020.
48. Alhussein MM, Mokbel A, Cosman T, et al. Pertuzumab cardiotoxicity in patients with HER2-positive cancer: a systematic review and meta-analysis. CJC Open. 2021;3(11):1372–82. https://doi.org/10.1016/j.cjco.2021.06.019.
49. Yoo JJ, Jung EA, Kim Z, Kim BY. Risk of cardiovascular events and lipid profile change in patients with breast cancer taking aromatase inhibitor: a systematic review and meta-analysis. Curr Oncol. 2023;30(2):1831–43. https://doi.org/10.3390/curroncol30020142.
50. Macedo AVS, Hajjar LA, Lyon AR, et al. Efficacy of dexrazoxane in preventing anthracycline cardiotoxicity in breast cancer. JACC: CardioOncology. 2019;1(1):68–79. https://doi.org/10.1016/j.jaccao.2019.08.003.
51. Omland T, Heck SL, Gulati G. The role of cardioprotection in cancer therapy cardiotoxicity. JACC: CardioOncology. 2022;4(1):19–37. https://doi.org/10.1016/j.jaccao.2022.01.101.
52. Cardwell CR, O'Sullivan JM, Jain S, et al. The risk of cardiovascular disease in prostate cancer patients receiving androgen deprivation therapies. Epidemiology. 2020;31(3):432–40. https://doi.org/10.1097/EDE.0000000000001132.
53. Leoce NM, Jin Z, Kehm RD, et al. Modeling risks of cardiovascular and cancer mortality following a diagnosis of loco-regional breast cancer. Breast Cancer Res. 2021;23(1):91. https://doi.org/10.1186/s13058-021-01469-w.
54. Kim DY, Park M, Youn J, et al. Development and validation of a risk score model for predicting the cardiovascular outcomes after breast cancer therapy: the CHEMO-RADIAT score. J Am Heart Assoc. 2021;10(16):e021931. https://doi.org/10.1161/JAHA.121.021931.
55. Liou L, Kaptoge S, Dennis J, et al. Genomic risk prediction of coronary artery disease in women with breast cancer: a prospective cohort study. Breast Cancer Res. 2021;23(1):94. https://doi.org/10.1186/s13058-021-01465-0.
56. Altena R, Hubbert L, Kiani NA, Wengström Y, Bergh J, Hedayati E. Evidence-based prediction and prevention of cardiovascular morbidity in adults treated for cancer. Cardio-Oncology. 2021;7(1):20. https://doi.org/10.1186/s40959-021-00105-y.
57. Galimzhanov A, Istanbuly S, Tun HN, et al. Cardiovascular outcomes in breast cancer survivors: a systematic review and meta-analysis. Eur J Prev Cardiol. 2023;30(18):2018–31. https://doi.org/10.1093/eurjpc/zwad243.
58. Zullig LL, Sung AD, Khouri MG, et al. Cardiometabolic comorbidities in cancer survivors: JACC: CardioOncology state-of-the-art review. JACC CardioOncol. 2022;4(2):149–65. https://doi.org/10.1016/j.jaccao.2022.03.005.
59. Deimling GT, Bowman KF, Wagner LJ. Cancer survivorship and identity among long-term survivors. Cancer Invest. 2007;25(8):758–65. https://doi.org/10.1080/07357900600896323.
60. Mayer DK, Nasso SF, Earp JA. Defining cancer survivors, their needs, and perspectives on survivorship health care in the USA. Lancet Oncol. 2017;18(1):e11–8. https://doi.org/10.1016/S1470-2045(16)30573-3.
61. Smith MR, Lee H, McGovern F, et al. Metabolic changes during gonadotropin-releasing hormone agonist therapy for prostate cancer: differences from the classic metabolic syndrome. Cancer. 2008;112(10):2188–94. https://doi.org/10.1002/cncr.23440.
62. Leong DP, Teo KK, Rangarajan S, et al. Prognostic value of grip strength: findings from the prospective Urban Rural Epidemiology (PURE) study. Lancet. 2015;386(9990):266–73. https://doi.org/10.1016/S0140-6736(14)62000-6.
63. Tsai HT, Keating NL, Van Den Eeden SK, et al. Risk of diabetes among patients receiving primary androgen deprivation therapy for clinically localized prostate cancer. J Urol. 2015;193(6):1956–62. https://doi.org/10.1016/j.juro.2014.12.027.
64. Wu YH, Jhan JH, Ke HL, et al. Risk of developing hypertension after hormone therapy for prostate cancer: a nationwide propensity score-matched longitudinal cohort study. Int J Clin Pharm. 2020;42(6):1433–9. https://doi.org/10.1007/s11096-020-01143-9.
65. Lear SA, Hu W, Rangarajan S, et al. The effect of physical activity on mortality and cardiovascular disease in 130 000 people from 17 high-income, middle-income, and low-income countries: the PURE study. Lancet. 2017;390(10113):2643–54. https://doi.org/10.1016/S0140-6736(17)31634-3.
66. Shao W, Zhang H, Qi H, Zhang Y. The effects of exercise on body composition of prostate cancer patients receiving androgen deprivation therapy: an update systematic review and meta-analysis. PLoS ONE. 2022;17(2):e0263918. https://doi.org/10.1371/journal.pone.0263918.

67. Kang DW, Fairey AS, Boulé NG, Field CJ, Wharton SA, Courneya KS. Effects of exercise on cardiorespiratory fitness and biochemical progression in men with localized prostate cancer under active surveillance: the ERASE randomized clinical trial. JAMA Oncol. 2021;7(10):1487–95. https://doi.org/10.1001/jamaoncol.2021.3067.

Publisher's note